ADME NTP Study K60344 Nickel sulfate hexahydrate

The contract laboratory abbreviation for the test article is NSHH.
Sex/Species: adult male F344/N rats.
Vehicles: intravenous, 0.9% saline; oral, 0.5 M H_2SO_4; inhalation, air.

CASRN 10101-97-0

Radiolabeled with ^{63}Ni as $^{63}NiCl_2$ which was incorporated into the aerosols of nickel sulfate hexahydrate.

Nickel sulfate hexahydrate Groups in Studies Performed:

- Subgroup A – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with sacrifice immediately after exposure (respiratory tract deposition). (Tables 2 and 3; n= 3)

- Subgroup B – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with sacrifice 10 to 13 days following exposure (excretion). (Tables 3 and 4; n= 3)

- Subgroup C – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with serial sacrifice to up to 64 days following exposure (tissue distribution). (Tables 5-21; n= 3 per timepoint)

Separate groups of rats (n=3 per group) were administered NSHH (4 ug Ni/rat) by gavage or intravenous injection to determine the gastrointestinal absorption of nickel. The data was presented in figures and not shown here. The gastrointestinal absorption from the gavage and intravenous injection routes was approximatedly 1.7%.

The activity median aerodynamic diameter (AMAD) ranged from 2.1 to 2.7 um, with geometric standard deviations of 1.7 to 1.9 (Table 1).

Subgroup A rats were equipped with individual plethysmographic units during the 1-hour exposure to measure respiratory parameters during exposure. The concentration of the material in the atmosphere, the volume of air inspired during exposure and the amount of ^{63}Ni deposited and absorbed following inhalation were determined. Respiratory measurements were corrected for body temperature and pressure, saturated.

Subgroup B rats were sacrificed 10-13 days after the 1-hour inhalation exposures. Urine and feces were collected at approximately 4, 7, 10, 16, 24, 48, 72, and 96 hours after exposure and then daily until the daily urine sample had no more than 1% of the cumulative activity in the urine. The average data is presented in figures and not shown here. Cumulative individual animal data (total nmoles deposited) is shown in Table 4. After all three inhalation exposures, feces was the dominant route for excretion of

nickel, representing from 80-85% of the deposited nickel. Urinary excretion of nickel accounted for 12-18% of the dose.

Subgroup C rats were sacrificed at different times after the end of the inhalation exposure (n=3 per timepoint). Nickel deposition was determined for tissues associated with the respiratory tract (including the skull primarily to determine disposition associated with the bony structures of the upper respiratory tract; Tables 5-9), tissues associated with the gastrointestinal tract (Tables 10-14), and internal organs including blood (Tables 15-21).

Appendix tables referenced in footnotes are in the original report and not shown here except for table 4 which is a copy of the Appendix Table E-3d.

Toxicokinetics:

The data for the concentration of nickel in tissues taken at necropsy were fit to the single-component exponential function $F(t) = Ae^{-Bt}$ where t is days after the end of exposure, A is percentage of deposited nickel per gram tissues, and B is the first order rate constant in 1/days. The associated half-time for clearance was calculated by using the following equation: $t_{½} = \ln 2/B$ where B is the first order rate constant, as described above. The half-times of clearances from tissues are shown in Tables 22-24.

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Table 1

Summary of Nickel Sulfate Hexahydrate Exposure Atmosphere in ^{63}Ni Toxicokinetic Studies

Target Concentration ($\mu g\ NiSO_4 \cdot 6H_2O/L$)	Actual Concentration[a] ($\mu g\ NiSO_4 \cdot 6H_2O/L$)	AMAD[b] (μm)	Geometric Standard Deviation[c] (σ_g)
1	0.735	2.3	1.8
3	1.96	2.7	1.9
12	11.7	2.1	1.7

[a]Determined by radioanalysis of a 60-minute, continuous filter sample.
[b]Activity median aerodynamic diameter, determined from samples taken during exposure from 2 Mercer cascade impactors.
[c]Geometric standard deviation of aerosol determined from Mercer cascade impactor measurements taken during the exposure.

Table 2

Total and Regional Fractional Deposition of ^{63}Ni After Exposure to Aerosols of Nickel Sulfate Hexahydrate[a]

Parameter	Exposure Concentration (μg $NiSO_4 \cdot 6H_2O$/L) 0.735	1.96	11.7
Ni Inhaled[b] (nmoles)	21.0 ± 3.3	77 ± 14	395 ± 15
Total Ni Deposited[c] (nmoles)	25.1 ± 5.3	29.34 ± 0.88	258.8 ± 9.4
(% of inhaled)	118.6 ± 6.7	42 ± 10	65.8 ± 3.8
Upper Respiratory Tract Deposition[d] (nmoles)	13.05 ± 0.35	20.56 ± 0.39	117.6 ± 4.7
(% of total deposited)	54 ± 10	70.2 ± 3.0	45.5 ± 1.2
Lower Respiratory Tract Deposition[e] (nmoles)	12.1 ± 5.0	8.7 ± 1.1	141.1 ± 6.7
(% of total deposited)	46 ± 10	29.7 ± 3.1	54.5 ± 1.2

[a]Data represent means ± SEM. Data for individual animals are in Appendix E, Tables E-1 and E-2.
[b]Ni inhaled is the product of the aerosol concentration (in nmoles/L) and the total volume inhaled (in liters).
[c]Total nickel deposited is the sum of nickel detected in the tissues represented in Figure 4, excluding pelt (i.e., nasal turbinates and skull, trachea and larynx, GI tract plus contents, lungs and bronchi, and carcass).
[d]Upper respiratory tract deposition includes nickel detected in the nasal turbinates and skull, trachea and larynx, and GI tract plus contents.
[e]Lower respiratory tract deposition includes nickel detected in lungs and bronchi and depelted carcass.

Table 3

Comparison of Total nmoles of Nickel Deposited in Rats After Exposure to Nickel Sulfate Hexahydrate Aerosols[a]

Exposure Concentration (µg/L)	Total nmoles Ni: Subgroup A Respiratory Tract Deposition[b]	Total nmoles Ni: Subgroup B Pathways for Excretion[c]
0.735	31.0 ± 3.9	31.6 ± 1.2
1.96	33.31 ± 0.58	37.0 ± 1.4
11.7	298 ± 13	236 ± 12

[a]Data represent mean ± SEM.
[b]Represents nickel detected in all tissues shown in Figure 4 including the pelt. Data for individual animals are in Appendix E, Tables E-3a, E-3b, and E-3c.
[c]Represents nickel detected in all excreta samples and carcass, as shown in Figure 6. Data for individual animals are in Appendix E, Table E-3d (Table 4 below).

Table 4

Total nmoles deposited in rats after exposure to Nickel Sulfate Hexhahydrate Aerosols

Subgroup B n=3

0.74 ug/l

TOTAL 15 Rats x 3C

	Exp-Tissue	Animal No.	nmoles	Total
1	4778 Urine	16	5.645149	33.926514
2		35	5.480803	30.213171
3		49	5.390568	30.548044
4	4778 Cagewash	16	0.041432	
5		35	0.010865	
6		49	0.022476	
7	4778 Feces	16	27.977474	
8		35	24.456025	
9		49	24.841919	
10	4778 Pelt	16	0.213545	
11		35	0.131650	
12		49	0.129178	
13	4778 Carass	16	0.048914	
14		35	0.133828	
15		49	0.163903	

1.96 ug/l

TOTAL 15 Rats x 3C

	Exp-Tissue	Animal No.	nmoles	Total
1	4777 Urine	8	4.831568	39.421007
2	4777 Cagewash	8	0.356610	
3	4777 Feces	8	33.620296	
4	4777 Pelt	8	0.376949	
5	4777 Carcass	8	0.435584	
6		26	4.599120	37.122642
7		26	0.036897	
8		26	31.659855	
9		26	0.339893	
10		26	0.486877	
11		51	4.236252	34.524045
12		51	0.027519	
13		51	29.759527	
14		51	0.245419	
15		51	0.355328	

11.7 ug/l

TOTAL 15 Rmts x 3C

	Exp-Tissue	Animal No.	nmoles	Total
1	Urine 4776	9	43.078729	257.101031
2		13	28.663020	214.295436
3		28	26.942193	237.142419
4	Cagewash 4776	9	0.568287	
5		13	0.727837	
6		28	0.806311	
7	Feces 4776	9	210.668611	
8		13	180.673212	
9		28	207.235524	
10	Pelt 4776	9	1.705005	
11		13	3.021819	
12		28	0.592065	
13	Carcass 4776	9	1.080399	
14		13	1.209548	
15		28	1.566326	

Table 5

Mean Percentage of Deposited Nickel Located in the Nasal Turbinates[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	3.26 ± 0.26	0.56 ± 0.22	4.36 ± 1.4
0.19	2.56 ± 0.84	2.09 ± 0.50	6.8 ± 3.5
0.35	3.5 ± 1.1	1.25 ± 0.54	2.18 ± 0.79
1.01	2.08 ± 0.48	1.07 ± 0.31	1.6 ± 0.41
2.01	1.13 ± 0.24	0.87 ± 0.36	0.84 ± 0.36
4.67	0.52 ± 0.16	0.349 ± 0.083	0.511 ± 0.071
8.00	0.344 ± 0.045	0.177 ± 0.042	0.43 ± 0.11
13.00	0.129 ± 0.013	0.153 ± 0.026	0.121 ± 0.055
16.00	0.19 ± 0.11	0.042 ± 0.012	0.136 ± 0.036
24.00	0.016 ± 0.016	0.072 ± 0.010	0.057 ± 0.023
31.00	0.0227 ± 0.0035	0.0158 ± 0.0014	0.061 ± 0.025
64.00	0.051 ± 0.020	0.0120 ± 0.0015	0.0250 ± 0.0045

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-4.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 6

Mean Percentage of Deposited Nickel Located in the Skull[a]
(not including brain)

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.12051 ± 0.00048	0.050 ± 0.016	0.165 ± 0.014
0.19	0.0701 ± 0.0048	0.083 ± 0.032	0.161 ± 0.030
0.35	0.097 ± 0.021	0.059 ± 0.018	0.082 ± 0.024
1.01	.0596 ± 0.0080	0.0346 ± 0.0087	0.0489 ± 0.0020
2.01	0.0267 ± 0.0047	0.0217 ± 0.0055	0.038 ± 0.011
4.67	0.0094 ± 0.0030	0.0105 ± 0.0024	0.0170 ± 0.0023
8.00	0.00794 ± 0.00080	0.0051 ± 0.0011	0.0188 ± 0.0049
13.00	0.00276 ± 0.00059	0.0069 ± 0.0011	0.0051 ± 0.0015
16.00	0.00222 ± 0.00025	0.00072 ± 0.00019	0.00230 ± 0.00073
24.00	0.00059 ± 0.00045	0.00289 ± 0.00053	0.0059 ± 0.0041
31.00	0.00113 ± 0.00013	0.00164 ± 0.00018	0.00197 ± 0.00047
64.00	0.00270 ± 0.00069	0.00200 ± 0.00059	0.00099 ± 0.00013

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-5.
[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 7

Mean Percentage of Deposited Nickel Located in the Trachea and Larynx[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	4.3 ± 1.6	1.57 ± 0.65	8.07 ± 1.4
0.19	3.25 ± 0.38	1.261 ± 0.072	3.82 ± 0.56
0.35	2.92 ± 0.64	1.66 ± 0.46	2.51 ± 0.63
1.01	1.127 ± 0.012	1.18 ± 0.66	2.25 ± 0.47
2.01	0.54 ± 0.16	0.46 ± 0.12	0.46 ± 0.23
4.67	0.236 ± 0.028	0.1383 ± 0.0054	0.156 ± 0.013
8.00	0.1309 ± 0.0039	0.0752 ± 0.0038	0.123 ± 0.034
13.00	0.048 ± 0.012	0.112 ± 0.011	0.038 ± 0.014
16.00	0.0371 ± 0.0017	0.0239 ± 0.0016	0.062 ± 0.020
24.00	0.0259 ± 0.0018	0.0510 ± 0.0054	1.1 ± 1.1
31.00	0.0227 ± 0.0026	0.0194 ± 0.0045	0.022 ± 0.011
64.00	0.0305 ± 0.0091	0.01231 ± 0.00027	0.0240 ± 0.0043

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-6.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 8

Mean Percentage of Deposited Nickel Located in the Lungs and Bronchi[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	8.9 ± 1.5	2.65 ± 0.67	18.3 ± 4.3
0.19	8.52 ± 0.37	4.2 ± 1.3	19.1 ± 6.2
0.35	5.44 ± 0.17	2.72 ± 0.84	10.9 ± 2.9
1.01	3.81 ± 0.94	2.49 ± 0.27	14.7 ± 1.6
2.01	1.503 ± 0.062	0.95 ± 0.10	6.2 ± 2.7
4.67	0.851 ± 0.082	0.495 ± 0.082	3.5 ± 1.6
8.00	0.345 ± 0.010	0.237 ± 0.026	0.736 ± 0.048
13.00	0.133 ± 0.018	0.145 ± 0.019	0.191 ± 0.035
16.00	0.082 ± 0.014	0.0640 ± 0.0063	0.159 ± 0.037
24.00	0.0222 ± 0.0031	0.0645 ± 0.0074	0.0615 ± 0.0099
31.00	0.0300 ± 0.0074	0.0207 ± 0.0037	0.0357 ± 0.0090
64.00	0.0370 ± 0.0041	0.0196 ± 0.0014	0.0152 ± 0.0030

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [Driginally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-7.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 9

Mean Percentage of Deposited Nickel Located in the Lung-Associated Lymph Nodes[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.30 ± 0.15	-0.040 ± 0.004	0.079 ± 0.048
0.19	0.146 ± 0.075	0.070 ± 0.070	0.101 ± 0.092
0.35	0.153 ± 0.085	0.138 ± 0.073	0.037 ± 0.010
1.01	0.065 ± 0.023	0.081 ± 0.088	0.110 ± 0.088
2.01	0.069 ± 0.025	0.155 ± 0.061	0.039 ± 0.059
4.67	0.037 ± 0.032	0.075 ± 0.027	0.130 ± 0.044
8.00	-0.0113 ± 0.0072	0.067 ± 0.037	0.37 ± 0.12
13.00	-0.053 ± 0.014	0.167 ± 0.026	0.41 ± 0.29
16.00	0.057 ± 0.048	-0.023 ± 0.030	1.17 ± 0.92
24.00	-0.059 ± 0.014	0.137 ± 0.052	0.215 ± 0.070
31.00	0.30 ± 0.12	0.065 ± 0.015	0.051 ± 0.042
64.00	0.098 ± 0.052	0.167 ± 0.039	0.0256 ± 0.0085

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-8.
[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 10

Mean Percentage of Deposited Nickel Located in the Esophagus[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	1.30 ± 0.29	0.89 ± 0.50	1.78 ± 0.87
0.19	0.412 ± 0.067	0.436 ± 0.044	0.67 ± 0.12
0.35	0.450 ± 0.074	0.297 ± 0.058	0.25 ± 0.10
1.01	0.0234 ± 0.0031	0.036 ± 0.011	0.122 ± 0.090
2.01	0.0163 ± 0.0025	0.0184 ± 0.0056	0.0081 ± 0.0018
4.67	0.00379 ± 0.00091	0.00588 ± 0.00049	0.0204 ± 0.0060
8.00	0.0040 ± 0.0020	0.0075 ± 0.0024	0.19 ± 0.10
13.00	0.0043 ± 0.0043	0.0271 ± 0.0035	0.0226 ± 0.0037
16.00	0.0075 ± 0.0030	0.0040 ± 0.0023	0.039 ± 0.012
24.00	-0.0009 ± 0.0026	0.0201 ± 0.0021	0.0130 ± 0.0071
31.00	0.0150 ± 0.0036	0.0075 ± 0.0018	0.0077 ± 0.0048
64.00	0.0163 ± 0.0066	0.0176 ± 0.0029	0.0071 ± 0.0024

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-9.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 11

Mean Percentage of Deposited Nickel Located in the Stomach[a] (without contents)

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.1060 ± 0.0088	0.0158 ± 0.0079	0.0471 ± 0.0094
0.19	0.040 ± 0.012	0.042 ± 0.034	0.0343 ± 0.0046
0.35	0.0258 ± 0.0044	0.0214 ± 0.0048	0.029 ± 0.011
1.01	0.0091 ± 0.0028	0.0043 ± 0.0044	0.039 ± 0.022
2.01	0.0064 ± 0.0027	0.0179 ± 0.0036	0.032 ± 0.028
4.67	0.0115 ± 0.0073	0.0090 ± 0.0011	0.032 ± 0.017
8.00	0.00189 ± 0.00070	0.00433 ± 0.00027	0.041 ± 0.027
13.00	-0.0005 ± 0.0013	0.0264 ± 0.0042	0.041 ± 0.034
16.00	0.00206 ± 0.00092	0.0023 ± 0.0036	0.028 ± 0.012
24.00	-0.00303 ± 0.00044	0.0273 ± 0.0024	0.0073 ± 0.0017
31.00	0.0199 ± 0.0036	0.0123 ± 0.0037	0.0090 ± 0.0062
64.00	0.0124 ± 0.0033	0.0165 ± 0.0034	0.00578 ± 0.00085

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [original17, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-10.
[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 12

Mean Percentage of Deposited Nickel Located in the Small Intestine[a] (without contents)

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.010 ± 0.033	0.042 ± 0.020	0.0332 ± 0.0049
0.19	0.0398 ± 0.0079	0.060 ± 0.053	0.065 ± 0.031
0.35	0.0176 ± 0.0040	0.0277 ± 0.0075	0.056 ± 0.022
1.01	0.0083 ± 0.0024	0.0104 ± 0.0058	0.030 ± 0.017
2.01	0.0049 ± 0.0029	0.0213 ± 0.0053	0.0019 ± 0.0010
4.67	0.0039 ± 0.0027	0.0176 ± 0.0065	0.028 ± 0.015
8.00	0.0019 ± 0.0022	0.0059 ± 0.0013	0.096 ± 0.022
13.00	-0.0017 ± 0.0018	0.0174 ± 0.0011	0.0112 ± 0.0063
16.00	0.0041 ± 0.0012	-0.00124 ± 0.00089	0.108 ± 0.039
24.00	-0.00329 ± 0.00089	0.0192 ± 0.0049	0.20 ± 0.19
31.00	0.0201 ± 0.0034	0.0100 ± 0.0022	0.0087 ± 0.0059
64.00	0.0168 ± 0.0028	0.0150 ± 0.0033	0.0077 ± 0.0040

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-11.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 13

Mean Percentage of Deposited Nickel Located in the Large Intestine[a] (without contents)

Days After End of Exposure[b]	Exposure Concentration (µg/L) 0.735	1.96	11.7
0.07	0.0370 ± 0.0019	0.0094 ± 0.0020	0.0266 ± 0.0046
0.19	1.12 ± 0.58	0.18 ± 0.17	0.29 ± 0.20
0.35	0.333 ± 0.064	0.065 ± 0.031	0.57 ± 0.16
1.01	0.150 ± 0.045	0.131 ± 0.044	0.175 ± 0.083
2.01	0.040 ± 0.026	0.0380 ± 0.0033	0.01839 ± 0.00044
4.67	0.0057 ± 0.0022	0.0174 ± 0.0014	0.022 ± 0.015
8.00	0.0035 ± 0.0021	0.0061 ± 0.0011	0.123 ± 0.046
13.00	0.0025 ± 0.0047	0.0251 ± 0.0021	0.0206 ± 0.0083
16.00	0.024 ± 0.021	0.0016 ± 0.0032	0.059 ± 0.030
24.00	-0.0029 ± 0.0017	0.0232 ± 0.0096	0.0162 ± 0.0033
31.00	0.0193 ± 0.0093	0.0101 ± 0.0034	0.0116 ± 0.0073
64.00	0.0124 ± 0.0018	0.0171 ± 0.0047	0.0051 ± 0.0010

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-12.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 14

Mean Percentage of Deposited Nickel Located in the Liver[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.101 ± 0.038	0.022 ± 0.021	0.0219 ± 0.0048
0.19	2.040 ± 2.021	0.0109 ± 0.0060	0.01426 ± 0.00076
0.35	0.0278 ± 0.0074	0.030 ± 0.016	0.035 ± 0.026
1.01	0.030 ± 0.011	0.0088 ± 0.0078	0.032 ± 0.027
2.01	0.0184 ± 0.0014	0.0378 ± 0.0027	0.0110 ± 0.0088
4.67	0.0237 ± 0.0074	0.0135 ± 0.0016	0.0119 ± 0.0039
8.00	0.0093 ± 0.0019	0.0127 ± 0.0023	0.108 ± 0.052
13.00	0.00211 ± 0.00075	0.0473 ± 0.0039	0.033 ± 0.018
16.00	0.0048 ± 0.0011	0.00364 ± 0.00080	0.076 ± 0.047
24.00	0.0023 ± 0.0010	0.0383 ± 0.0073	0.0127 ± 0.0046
31.00	0.033 ± 0.017	0.0139 ± 0.0014	0.025 ± 0.018
64.00	0.047 ± 0.011	0.0167 ± 0.0025	0.0138 ± 0.0014

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-13.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 15

Mean Percentage of Deposited Nickel Located in Whole Blood[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	1.42 ± 0.96	0.037 ± 0.019	0.0437 ± 0.0026
0.19	0.28 ± 0.12	0.018 ± 0.013	0.0374 ± 0.0067
0.35	0.41 ± 0.33	0.027 ± 0.010	0.049 ± 0.018
1.01	0.19 ± 0.12	0.0219 ± 0.0044	0.0253 ± 0.0046
2.01	0.124 ± 0.030	0.0316 ± 0.0035	0.0090 ± 0.0028
4.67	0.133 ± 0.059	0.0177 ± 0.0012	0.0242 ± 0.0043
8.00	0.0806 ± 0.0065	0.0265 ± 0.0036	0.055 ± 0.027
13.00	0.025 ± 0.014	0.055 ± 0.010	0.052 ± 0.029
16.00	0.0376 ± 0.0046	0.0127 ± 0.0040	0.044 ± 0.017
24.00	0.0064 ± 0.0018	0.0294 ± 0.0075	0.043 ± 0.015
31.00	0.0240 ± 0.0018	0.026 ± 0.012	0.107 ± 0.056
64.00	0.0116 ± 0.0014	0.0216 ± 0.0030	0.0438 ± 0.0076

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here](Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-14.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 16

Mean Percentage of Deposited Nickel Located in the Adrenal Glands[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.0702 ± 0.0075	0.0068 ± 0.0034	0.061 ± 0.042
0.19	0.0302 ± 0.0084	0.0152 ± 0.0077	0.030 ± 0.012
0.35	0.021 ± 0.012	0.022 ± 0.012	0.0134 ± 0.0024
1.01	0.0314 ± 0.0038	0.0078 ± 0.0086	0.056 ± 0.044
2.01	0.0158 ± 0.0055	0.0433 ± 0.0063	0.058 ± 0.050
4.67	0.0059 ± 0.0017	0.0196 ± 0.0079	0.0453 ± 0.0052
8.00	0.0099 ± 0.0032	0.0070 ± 0.0022	0.118 ± 0.061
13.00	0.0088 ± 0.0060	0.0415 ± 0.0052	0.081 ± 0.069
16.00	0.0098 ± 0.0047	0.0039 ± 0.0027	0.175 ± 0.083
24.00	-0.0065 ± 0.0036	0.026 ± 0.011	0.0133 ± 0.0014
31.00	0.0205 ± 0.0048	0.0071 ± 0.0023	0.032 ± 0.022
64.00	0.048 ± 0.016	0.0155 ± 0.0073	0.0157 ± 0.0020

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here](Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-15.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 17

Mean Percentage of Deposited Nickel Located in the Thyroid Glands[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.33 ± 0.19	0.003 ± 0.011	0.51 ± 0.34
0.19	0.116 ± 0.069	0.020 ± 0.020	0.046 ± 0.016
0.35	0.063 ± 0.024	0.088 ± 0.044	0.16 ± 0.14
1.01	0.135 ± 0.053	0.045 ± 0.040	0.049 ± 0.027
2.01	0.036 ± 0.034	0.0263 ± 0.0079	0.0027 ± 0.0095
4.67	0.0101 ± 0.0023	0.0435 ± 0.0038	0.098 ± 0.052
8.00	0.0112 ± 0.0067	0.0329 ± 0.0031	0.94 ± 0.67
13.00	-0.008 ± 0.012	0.137 ± 0.028	0.96 ± 0.20
16.00	0.024 ± 0.017	-0.010 ± 0.014	0.120 ± 0.040
24.00	-0.0263 ± 0.0020	0.0764 ± 0.0042	0.076 ± 0.050
31.00	0.0724 ± 0.0099	0.095 ± 0.022	0.066 ± 0.042
64.00	0.045 ± 0.018	0.118 ± 0.068	0.0311 ± 0.0031

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-16.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 18

Mean Percentage of Deposited Nickel Located in the Testes[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	0.01982 ± 0.00056	-0.0022 ± 0.0015	0.0159 ± 0.0021
0.19	0.035 ± 0.016	0.0076 ± 0.0044	0.019 ± 0.010
0.35	0.0190 ± 0.0069	0.0101 ± 0.0050	0.0134 ± 0.0045
1.01	0.0127 ± 0.0035	0.0018 ± 0.0028	0.036 ± 0.027
2.01	0.022 ± 0.018	0.0200 ± 0.0017	0.0006 ± 0.0010
4.67	0.00077 ± 0.00044	0.00783 ± 0.00072	0.026 ± 0.012
8.00	-0.00079 ± 0.00021	0.0061 ± 0.0013	0.0183 ± 0.0079
13.00	-0.0016 ± 0.0021	0.0238 ± 0.0040	0.145 ± 0.060
16.00	0.00205 ± 0.00032	-0.0012 ± 0.0029	0.079 ± 0.029
24.00	-0.0046 ± 0.0017	0.0264 ± 0.0080	0.0105 ± 0.0046
31.00	0.0167 ± 0.0012	0.01003 ± 0.00063	0.0055 ± 0.0047
64.00	0.0155 ± 0.0018	0.0168 ± 0.0018	0.0046 ± 0.0014

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-17.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 19

Mean Percentage of Deposited Nickel Located in the Kidneys[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L) 0.735	1.96	11.7
0.07	0.299 ± 0.021	0.037 ± 0.013	0.102 ± 0.029
0.19	0.158 ± 0.038	0.121 ± 0.030	0.174 ± 0.058
0.35	0.281 ± 0.034	0.107 ± 0.018	0.118 ± 0.033
1.01	0.122 ± 0.037	0.059 ± 0.014	0.081 ± 0.016
2.01	0.151 ± 0.098	0.060 ± 0.010	0.097 ± 0.019
4.67	0.0435 ± 0.0061	0.0404 ± 0.0070	0.0579 ± 0.0052
8.00	0.0372 ± 0.0044	0.0209 ± 0.0010	0.117 ± 0.038
13.00	0.027 ± 0.014	0.072 ± 0.021	0.046 ± 0.019
16.00	0.035 ± 0.026	0.0322 ± 0.0048	0.0287 ± 0.0059
24.00	0.0068 ± 0.0032	0.055 ± 0.012	0.028 ± 0.012
31.00	0.0325 ± 0.0016	0.0167 ± 0.0017	0.054 ± 0.019
64.00	0.047 ± 0.013	0.0255 ± 0.0029	0.01026 ± 0.00066

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here](Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-18.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 20

Mean Percentage of Deposited Nickel Located in the Urinary Bladder[a] (without contents)

Days After End of Exposure[b]	Exposure Concentration (µg/L) 0.735	1.96	11.7
0.07	0.22 ± 0.12	0.0065 ± 0.0030	0.112 ± 0.042
0.19	0.0824 ± 0.0082	0.0307 ± 0.0044	0.078 ± 0.024
0.35	0.062 ± 0.017	0.087 ± 0.047	0.063 ± 0.031
1.01	0.0333 ± 0.0059	0.0081 ± 0.0071	0.096 ± 0.067
2.01	0.0067 ± 0.0036	0.0201 ± 0.0083	0.0057 ± 0.0034
4.67	0.0047 ± 0.0045	0.0133 ± 0.0059	0.047 ± 0.024
8.00	0.0003 ± 0.0016	0.0070 ± 0.0018	0.22 ± 0.14
13.00	0.0030 ± 0.0077	0.0347 ± 0.0037	0.308 ± 0.014
16.00	0.0104 ± 0.0068	0.0015 ± 0.0048	0.111 ± 0.076
24.00	-0.0083 ± 0.0049	0.0224 ± 0.0034	0.062 ± 0.025
31.00	0.0214 ± 0.0085	0.0087 ± 0.0021	0.017 ± 0.018
64.00	0.0184 ± 0.0079	0.0216 ± 0.0054	0.0137 ± 0.0042

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here](Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-19.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 21

Mean Percentage of Deposited Nickel Located in the Urine Contained in the Urinary Bladder[a]

Days After End of Exposure[b]	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
0.07	2.830 ± 0.030	0.90 ± 0.42	1.7513 ± 0.5829
0.19	2.006 ± 0.041	0.93 ± 0.11	1.5681 ± 0.3576
0.35	2.245 ± 0.069	1.01 ± 0.25	0.9713 ± 0.1958
1.01	0.216 ± 0.025	0.24 ± 0.13	0.5920 ± 0.1561
2.01	0.0889 ± 0.0097	0.028 ± 0.013	0.3010 ± 0.1469
4.67	0.030 ± 0.014	0.0105 ± 0.0056	0.128 ± 0.060
8.00	0.0058 ± 0.0024	0.0082 ± 0.0034	0.044 ± 0.015
13.00	0.0035 ± 0.0013	0.00023 ± 0.00061	0.0167 ± 0.0061
16.00	0.00131 ± 0.00049	-0.015 ± 0.013	0.0118 ± 0.0098
24.00	-0.0014 ± 0.0045	0.0069 ± 0.0024	0.40 ± 0.39
31.00	0.0139 ± 0.0049	0.0055 ± 0.0036	-0.0103 ± 0.011
64.00	-0.0034 ± 0.0032	0.0100 ± 0.0063	-0.0072 ± 0.0065

[a]Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-20.

[b]Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).

Table 22

Half-Times for Elimination of Nickel from the Respiratory Tract After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate[a]

Tissue	Exposure Concentration (µg/L) 0.735	1.96	11.7
Turbinates	1.6 (19)	3.0 (50)	0.55 (42)
Skull (brain removed)	1.1 (22)	1.3 (30)	0.55 (25)
Trachea	0.53 (8.7)	1.4 (19)	0.16 (25)
Lung	0.73 (14)	1.5 (27)	1.7 (24)
Lung-Associated Lymph Nodes	--[b]	--	--

[a]Data represent half-times in days with percent standard error in parentheses.
[b]Could not be determined, because of the low levels of activity in this tissue.

Table 23

Half-Times for Elimination of Nickel from the Gastrointestinal Tract and Liver After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate[a]

Tissue	Exposure Concentration (µg/L)		
	0.735	1.96	11.7
Esophagus	0.12 (17)	0.15 (8.1)	0.091 (10)
Stomach[b]	0.11 (22)	--[c]	--[c]
Small Intestine[b]	0.11 (22)	2.0 (70)	--[c]
Large Intestine[b]	0.82 (120)	2.9 (89)	1.7 (100)
Liver	0.46 (150)	--[c]	--[c]

[a]Data represent half-times in days with percent standard error in parentheses.
[b]Not including contents.
[c]Could not be determined, because of the low levels of activity in this tissue.

Table 24

Half-Times for Elimination of Nickel from the Internal Organs and Blood After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate[a]

Tissue	Exposure Concentration (µg/L) 0.735	1.96	11.7
Blood	0.074 (26)	--[b]	--[b]
Thyroids	0.094 (39)	--[b]	--[b]
Adrenals	1.1 (96)	--[b]	--[b]
Testes	2.0 (73)	--[b]	--[b]
Kidneys	2.0 (38)	23 (64)	13 (38)
Bladder[c]	0.12 (19)	28 (160)	60 (170)
Urine[d]	0.39 (7.7)	0.46 (31)	0.59 (23)

[a]Data represent half-times in days with percent standard error in parentheses.
[b]Could not be determined, because of the low levels of activity in this tissue.
[c]Not including contents.
[d]Present in the bladder at sacrifice.